Reprinted for the Author from the British Medical Journal, Feb. 15, 1890

REPORT ON THE VALUE OF SODIUM SILICOFLUORIDE AS AN ANTISEPTIC.[1]

By T. JESSOPP BOKENHAM, M.R.C.S., L.R.C.P.

For some years it has been an accepted idea among medical men that in antiseptics they would at length find the means of combating infective diseases (that is, those due to specific organisms). Experiments made by Dr. Theodore Cash, F.R.S.,[2] showed that corrosive sublimate, when administered to guinea pigs, would afford protection from anthrax, the animals under certain conditions living quite unaffected by the inoculation. The danger here lay, however, in the extremely poisonous nature of the antiseptic itself, and it has been a desideratum to find a less dangerous substitute.

Such, I thought, might be the silicofluoride of sodium which was introduced to my notice some months back by Messrs. Burroughs, Wellcome, and Co. With regard to this substance the following particulars may be interesting, as they formed the basis of my subsequent work. It was introduced by Mr. Wm. Thomson, F.R.S.E., who, in a paper before the British Association in 1888, claimed that it was a powerful antiseptic, non-volatile, colourless, sparingly soluble in water, neutral, and above all, non-poisonous. Its saturated aqueous solution, 0.61 per cent., was unirritating, although large doses of the solid acted as an emetic. However, as much as 7 grains had been taken as a dose, though perhaps it was not desirable to take more than ½ to 1 grain. Its antiseptic properties were demonstrated by adding the salt (1 to 700) to flour paste, or 1 to 200 to an infusion of chopped meat in water. The mixtures were placed in an incubator, and watched. After several days they were entirely free from either mould or decomposition. This was a more successful result than could be obtained with corrosive sublimate (1 to 500). The salt acted like alcohol in retarding the action of pepsin in albuminous bodies.

Mr. Robson, F.R.C.S.,[3] used the drug as an antiseptic in a great variety of surgical cases, and considered it specially useful in those cases in which there might be risk from absorption, if mercuric chloride were used.

Dr. Conrad Berens[4] found a solution of 1 to 1,000 strong enough to prevent all decomposition of vegetable and meat infusions, even when these were exposed for some weeks. He also found that a dose of 10 gr. in ℥iv of water could be borne without inconvenience, taken on an empty stomach and repeated three times daily for seven days.

After reading these accounts, I thought it would be interesting to undertake a series of experiments on the germicidal value of the substance given internally, working on the lines of Dr. Cash,[5]

[1] The expenses of this research were defrayed by the Therapeutic Committee of the British Medical Association.
[2] Report on Certain Chemical Disinfectants.
[3] Journal, May, 1888.
[4] *Therap. Gaz.*, 1888, p. 443.
[5] *Loc. cit.*

who found that a solution of mercuric chloride administered to an animal would protect it from the effects of a subsequent inoculation with anthrax. Before, however, undertaking this Dr. Brunton suggested that it would be well to first test the action of the drug on fermentation. This I proceeded to do. I took four flasks, and filled them as follows: Flask 1 contained 8 oz. glucose solution in water, sp. gr. 1040 at 15° C.; Flask 2 contained 8 oz. glucose solution in Na_2 Si F_6 soln. (1 to 150), sp. gr. 1040 at 15° C.; Flask 3 contained 8 oz. glucose solution in Na_2 Si F_6 soln. (1 to 300), sp. gr. 1040 at 15 C.; Flask 4 contained 8 oz. glucose solution in Na_2 Si F_6 soln. (1 to 600), sp. gr. 1040 at 15° C. To each I added a definite quantity of fresh yeast, and then plugged the necks, placing the flasks in an incubator at temperature 25° C. The specific gravities were taken every twenty-fours during seven days. It was thus found that the solution in Flask 1 became of lower specific gravity, whilst that in the others remained unchanged.

In experimenting with weaker solutions I adopted another method. A number of tubes of equal length and calibre were taken. These were filled with solutions of Na_2 Si F_6 of various strengths, each containing besides equal weights of glucose. Some actively growing yeast was then added; the tubes were inverted over pure mercury and placed in an incubator. The volume of CO_2, formed by the fermentation could thus be observed from day to day. The result is shown in the accompanying table:—

From these experiments it will be seen that a solution of Na_2 Si F_6 (1 to 750) will entirely prevent alcoholic fermentation; that solutions (1 to 900 and 1 to 1,050) will delay fermentation for a time, but that these latter cannot be considered truly antiseptic, as the growth of the yeast was only delayed.

[Experiments just lately performed with nutrient gelatine containing Na_2 Si F_6 (1 to 3,000 and 1 to 2,000) have shown that this proportion is quite without effect on the growth of the bacillus anthracis, and that there is no diminution in the virulence of bacilli cultivated through several generations on this pabulum.]

I next proceeded to try the effect of prolonged administration of the drug to guinea pigs.

Experiment I.—A saturated tepid solution of Na_2 Si F_6 was made in saline solution, 75 per cent., and of this 4 cubic centimètres were injected into the peritoneal cavity of a guinea pig (weight 1 lb. 14 oz.). A short time after the injection it was found with abdomen rigid and legs thrown out; temperature 38° C. in rectum. In spite of all efforts to recover the animal, it became collapsed, with temperature 26.5° C., and abdomen intensely tender. I then killed the animal, and found marked signs of peritonitis. No injury could be found attributable to the puncture of the syringe.

Experiment II.—Guinea pig (weight 10 oz.) 0.033 grammes, in warm saturated solution, were injected into the stomach with an œsophageal tube. Animal evinced uneasiness soon after injection; its abdomen became much distended, and it died after fifty-five minutes. *Post-mortem* appearances as follows: Stomach much dilated, with vessels injected; no signs of injury by the tube; full of pulpy food, with much thick mucus and gas. Intestines contained similar mucus. Heart arrested in diastole. Other organs normal.

Experiment III.—Guinea pig (female). On April 24th, injected 0.02 grammes in solution (1 to 300) into stomach. In three hours repeated the dose. April 25th. Animal quite well and lively. Injected during the day 0.1 gramme of the salt. April 26th. Again injected 0.1 gramme. April 27th. Animal quiet but feeds well. Injected 0.05 gramme in a single dose. Three hours

TABLE.

Tubes $6\frac{1}{2}$ inches. Yeast fresh, in active growth.

Tube No.	Proportion of Na_2SiF_6.	Day 1.	Day 2.	Day 3.	Day 4.	Day 5.	Day 6.	Day 7.	Day 8.	Day 9.	Day 10.	Day 11.	Day 12.
1	Control	3 in.	6 in.	*	—	—	—	—	—	—	—	—	—
2	Satd. 1 : 150	0	0	†	—	—	—	—	—	—	—	—	—
3	$\frac{1}{2}$ satd. 1 : 300	0	0	†	—	—	—	—	—	—	—	—	—
4	$\frac{1}{4}$ satd. 1 : 600	0	0	†	—	—	—	—	—	—	—	—	—
5	$\frac{1}{5}$ satd. 1 : 750	0	0	†	—	—	—	—	—	—	—	—	—
6	$\frac{1}{6}$ satd. 1 : 900	Small bubble	—	—	—	—	Large bubble	Not observed	6 in.	*	—	—	—
7	$\frac{1}{7}$ satd. 1 : 1050	Large bubble	—	—	—	—	—	1 in.	—	4 in.	6 in.	*	—
8	$\frac{1}{8}$ satd. 1 : 1200	2 bubbles	2 bub.	4 bub.	4 bub.	—	—	—	—	$4\frac{3}{4}$ in.	—	Empty	—
9	§ $\frac{1}{12}$ satd. 1 : 1800	1 bubble	—	—	—	—	—	2 bubbles	—	$1\frac{1}{2}$ in.	3 in.	$4\frac{1}{2}$ in.	5 in.‡
10	§ 1 : 7750	1 bubble	$\frac{1}{2}$ in.	3 in.	—	—	Empty	—	—	—	—	—	—

Completely fermented. † No fermentation. ‡ Completely fermented; control empty on sixth day. § Separate control tube for these two experiments.

afterwards it appeared uneasy, with some swelling of abdomen. Respiration became slow and laboured, and the animal seemed collapsed; temperature, 33° C. Shortly after this it died. *Post-mortem* appearances exactly as in Experiment II.

After this experience I had grave doubts as to the utility of trying further the internal administration of the drug. Still, I wished to control the statement as to its harmless nature when taken internally by man. My friend, Mr. Blackman, and I had noticed after drinking some of the saturated solution a feeling of distension of the stomach, with tendency to eructations, but had not thought of attributing these effects to the drug.

On April 28th, after a mixed meal, I took 0.05 gramme of the solid. I did not notice any effects for an hour, but, about that time after, a feeling of great nausea with eructations came on. This lasted several hours, and I felt utterly unable to do anything; the pulse was at the same time greatly slowed, tension being reduced. Next day all symptoms had passed off. Three of my friends, medical students, agreed to repeat my experiment on themselves. Each took a dose of 0.05 gramme, and the same feeling of nausea with eructations followed; the effects did not, however, last so long as in my case.

I think the above facts were sufficient to justify my abandoning the research. It is strange that my results did not tally with those of other observers, as I used a salt of great purity, and apparently identical in all respects with the one previously used.

In conclusion, I have to offer my best thanks to Dr. Lauder Brunton for his valuable advice, as well as for the use of his laboratory; and to Messrs. Burroughs, Wellcome, and Co. for the pains they took in procuring me an absolutely pure salt.

I feel that no apology is due for the appearance of the foregoing notes, as sodium silicofluoride seems to have been somewhat widely advertised, and I have frequently been asked whether it is a safe internal remedy. My experience will, at any rate, make others hesitate before they advise its use internally.